

## Cutaneous Cryptococcosis in a Patient with Cirrhosis and Hepatitis C Virus Infection

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Sir,

Cryptococcosis is a *Cryptococcus neoformans* fungal infection that occurs in immunocompromised patients. Cryptococcosis appears as meningitis, pneumonia, and cutaneous eruptions. Meningitis is regarded as the most common presentation, and is sometimes fatal to immunocompromised hosts. Hepatic cirrhosis due to infection with hepatitis C virus (HCV) is a disease known to lead to immunodeficiency. We report here a case of cutaneous cryptococcosis in an immunosuppressed patient with HCV.

### CASE REPORT

A 47-year-old Japanese man who had had HCV infection for 20 years had been diagnosed with cirrhosis some years previously. He had received interferon therapy for 6 months in 1992 and 2005, respectively. He was a farmer, and had no history of contact with pigeons. He had developed cellulitis four times, leading to admission to our hospital. In December 2007, he was again admitted to our hospital with fever and infiltrative erythema on the right lower leg (Fig. 1). Due to a suspicion of cellulitis, systemic antibiotics were administered, but were not effective. Infiltrative redness spread to the bilateral thighs, left forearm, and abdomen. He developed headache and cough, which gradually worsened. A biopsy specimen revealed dense granulomatous inflammation infiltrated by a number of neutrophils and lymphohistiocytic cells in the dermis to subcutaneous tissues. Numerous rounded bodies surrounded by a capsule were found in the dermis (Fig. 2a).



Fig. 1. Diffuse indurated erythema of the right lower leg.

The body of the yeast and the capsule were positively stained with periodic acid-Schiff (PAS), Alcian blue and mucicarmine which stains the body of *Cryptococcus* specifically (Fig. 2b). Laboratory examination revealed anaemia, liver and renal dysfunction, elevated levels of C-reactive protein (CRP) and  $\beta$ -D glucan. Cryptococcal antigen test was performed on serum, and showed positive. A human immunodeficiency virus (HIV) test was negative. Examination by computed tomography (CT) scanning showed bilateral pleural effusion and dissemination to the brain. Neurological manifestation involving the central nervous system appeared, and meningitis developed. Cultures from blood, cerebrospinal fluid (CSF) and urine all yielded *C. neoformans*. Polymerase chain reaction (PCR) analysis by specific fungal 18sRNA gene and *C. neoformans* genome (D1D2, ITS) using obtained colonies detected positive bands. The patient was treated with systemic amphotericin B and fluconazole, but died of sepsis.

### DISCUSSION

The clinical features of cutaneous cryptococcosis are papules, nodules, granulomas and ulcerations, occasionally resembling cellulitis, bullous erysipelas, or whitlow (1). Because our case had repetitively developed cellulitis, and showed a typical clinical appearance on admission, a biopsy was not carried out. However, infiltrative redness increased in spite of treatment with systemic antibiotics, and a skin biopsy was eventually performed. Histological and mycological examination led to a diagnosis of cryptococcosis. *Cryptococcus* infection sometimes involves not only skin, but also the lungs and central nervous system, and thus is life-threatening, especially in immunoincompetent individuals. Our case was infected in multiple organs, and antimycotic therapies were unsuccessful.

Cutaneous cryptococcosis is an opportunistic infection, and occasionally involves immunosuppressed hosts, such as patients with HIV infection, lymphomas, systemic lupus erythematosus, and transplant recipients under immunosuppressive therapies (2–5). Like our patient, cases of cutaneous cryptococcosis simulating bacterial cellulitis in immunocompetent hosts have been reported (5–8). Our patient had cirrhosis, and was thought to be in an immunosuppressive state. This is the first case of cutaneous cryptococcosis reported in a patient with HCV infection.

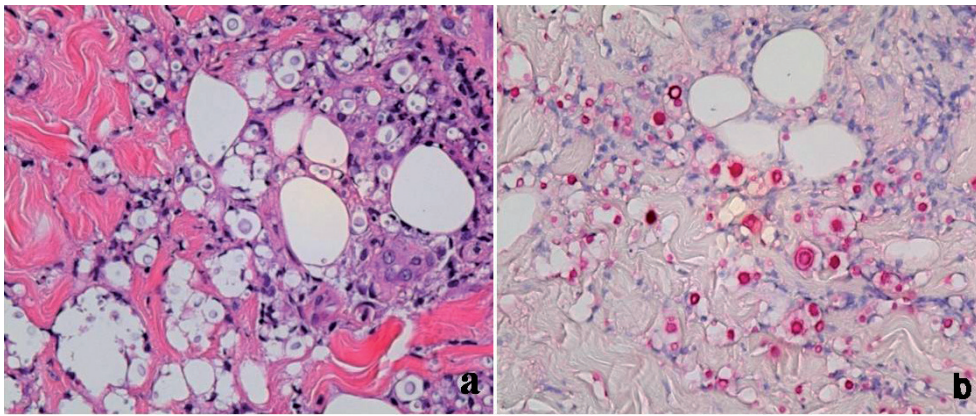


Fig. 2. Biopsy specimen from the abdomen. A number of spores with thick-walled capsules are visible. (a) Haematoxylin-eosin,  $\times 20$ ; (b) mucicarmine ( $\times 200$ ) staining.

Cutaneous cryptococcosis is more often secondary than primary. In the present case, it was difficult to determine whether it was primary or secondary. The patient repetitively developed cellulitis, and was supposedly easily affected by percutaneous infection of the yeast.

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